and 37 C.F.R. 1.141. It is suggested that compounds of claim 1 are targeted to different target regions of SEQ ID NO: 3. Claim 1 claims a compound targeted to a 5' untranslated region, a coding region, a stop codon region, or a 3' untranslated region of a nucleic acid molecule of SEQ ID NO:3 which are targeted to a nucleic acid encoding human fibroblast growth factor 2. Although the compounds claimed each target the expression of the same gene the compound targeting the recited target region sequences are considered to be unrelated. It is suggested that each compound has a unique sequence corresponding to the recited target region, each compound targets a different and specific region of a nucleic acid encoding human fibroblast growth factor 2, and each compound upon binding to a nucleic acid encoding human fibroblast growth factor 2 functionally modulates the expression of the gene and to varying degrees. Furthermore a search of more than one of the target region sequences of claim 1 is suggested to present an undue burden on the Patent Office.

In further support of the restriction requirement, it is suggested that where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806, the Examiner in order to establish reasons for insisting upon restriction must show an

appropriate explanation including that a different field of search is necessary.

The Examiner suggests that a search of the available sequence databases produces a listing of references disclosing the sequence most similar to the query sequence (target region). This is suggested to be the place where the Examiner searches for prior art. The prior art relating to another query sequence will not be found in this "place". Thus, it is suggested that a different search must be originated.

Applicants respectfully traverse this restriction requirement.

First, the MPEP §803 is quite clear; for a proper restriction requirement, it must be shown (1) that the inventions are independent or distinct AND (2) that there would be a serious burden on the Examiner if the restriction is not required. MPEP 802.01 defines "distinct" to mean that the "two or more subjects as disclosed are related, for example, as combination and part (subcombination) thereof, process and apparatus for its practice, process and product made there, etc., but are capable of separate manufacture, use, or sale, as claimed, AND ARE PATENTABLE (novel and unobvious) OVER EACH OTHER."

As acknowledged by the Examiner, all of claims of the instant application relate to the concept of modulation of fibroblast

growth factor receptor 2 expression. Accordingly, each of the claims contain the components for use in the same endpoint, namely the modulation of the same gene, SEQ ID NO: 3. Thus, Applicants respectfully disagree that the Groups set forth by the Examiner are distinct as being novel and unobvious over each other, as required by MPEP § 802.01.

Additionally, a search of literature relating to any one of target regions claimed in claim 1 of the instant invention would necessarily include the entire sequence of human growth factor receptor 2, SEQ ID NO:3, in preparation for the first Office action. The Applicants' interest in claiming only several, specific target regions of the SEQ ID NO:3, as reflected in the subsequent amendment, does nothing to alter the search burden placed on the Office, as the entire sequence had already been necessarily searched by the Examiner. The MPEP sets forth search guidelines for its Examiners. MPEP §904 states "[the first search should be such that the examiner need not ordinarily make a second search of the prior art, unless necessitated by amendments to the claims by the applicant in the first reply, except to check to determine whether any reference which would appear to be substantially more pertinent than the prior art cited in the first Office action has become available subsequent to the initial prior

art search. The first search should cover the invention as described and claimed, including the inventive concepts toward which the claims appear to be directed. It should not be extended merely to add immaterial variants."

Second, under MPEP 803, an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP §§806.04 - §§ 806.04(I)) or distinct (MPEP §§ 806.05 - §§806.05(I)). If the search and examination of an entire application can be made without serious burden, the examiner *must* examine it on the merits, even though it includes claims to independent or distinct inventions. All of the compounds of claim 1 share the technical feature of modulating the expression of human growth factor receptor 2 expression, thus examination and search requirements would not cause serious burden on the Office if the restriction requirement is not imposed.

Additionally, the MPEP §803.04, states that "to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR §1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See

Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996). It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together. In some exceptional cases, the complex nature of the claimed material, for example a protein amino acid sequence reciting three dimensional folds, may necessitate that the reasonable number of sequences to be selected be less than ten."

As recited in the Official Gazette 1192 O.G. 68 (November 19, 1996), "the PTO believes that allowing applicants to claim up to ten (10) independent and distinct nucleotide sequences in a single application will promote efficient, cost-effective examination of these types of applications". The Commissioner's *sua sponte* actions in allowing up to ten sequences to be examined in one application were intended to benefit both the biotechnology

industry and the Patent Office. Inclusion of up to ten related sequences in one application benefits the inventors by preventing the monetary detriment of filing multiple divisional applications for individual related sequences. The Patent Office is further benefitted by allowing examination of up to ten related individual sequences in one application as paperwork and administrative burden are greatly diminished.

Accordingly, restricting the sequences of claim 1 into target regions of multiple individual applications for examination is contrary to the intent of the Commissioner to provide efficient, cost-effective examination of inventions relating to biotechnology inventions comprising nucleotide sequences. Therefore, Applicants respectfully request that the restriction requirement be reconsidered and withdrawn.

However, in an earnest effort to be completely responsive, Applicants elect compounds targeted to the coding region of SEQ ID NO:3, with traverse.

Respectfully submitted,

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